IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Scott R. Presnell, Steven K. Burkhead, Sarah L. Powander
Serial No.	:	09/608,918
Filed	:	June 30, 2000
For	:	INTERLEUKIN-17 RECEPTOR HOMOLOGUE (As Amended)
Examiner	:	Prasad, S.
Art Unit	:	1646
Docket No.	:	99-50
Date	:	December 17, 2002

Commissioner for Patents
Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. §1.132

Sir:

I, Julia E. Parrish-Novak, declare and say as follows:

1. I received a B.S. in Biology and Chemistry from the University of Houston, Houston, Texas, in 1988, and Ph.D. in Biology from the University of Houston, Houston, Texas, in 1992. I had a postdoctoral fellowship at the Human Genome Center, Baylor College of Medicine, from September 1992 to January 1997. Since February 1997, I have been a scientist at Zymogenetics, Seattle, Washington in the following positions: Scientist (1997-1999), Senior Scientist (1999-2001), and Principal Scientist (2001-present).

2. My research activities include, but are not limited to, the study of cytokine receptor genes and the identification and characterization of their cognate ligands. I have several publications and have been invited to speak at numerous symposia on these and other related topics.

3. I have read and am familiar with the Office Action mailed June 17, 2002 with respect to the above-identified application, and make this Declaration in support of the patentability of the claims of patent application Serial No. 09/608,918.

4. The specification of patent application Serial No. 09/608,918 provides, for example, at page 70, lines 13-20, that zcytor14 may play a role in initiating or sustaining inflammation. The specification also provides, for example, at page 70, lines 20-24, that a soluble zcytor14 receptor may be used to inhibit inflammation.

5. RNA was isolated from zcytor14 (SEQ ID NOs:2 and10) and control vector transfected human embryonic kidney 293 cells. Gene expression profiling on the isolated RNA was carried out using GEArray Q series cDNA expression arrays. Comparison of arrays from treated and control cells allows for determination of the up- and down-regulation of specific genes.

6. Results of the gene expression arrays showed a significant up-regulation of several cytokines and receptors in the zcytor14 transfected 293 cell line, which include, but are not limited to, Interleukin-13 (IL-13), Fibroblast Growth Factor 6 (FGF-6), Transforming Growth Factor-alpha (TGF-alpha), Interleukin-12 receptor, beta 1 (IL-12Rbeta1), Interleukin-15 receptor alpha (IL-15R-alpha), and Interleukin-17 receptor (IL-17R).

7. IL-17 has been shown to be involved in both inflammation of the human airway (Jones et al., Am. J. Respir. Cell Mol. Biol., 26(6):748-753 (June 2002)) and in the development of bone lesions and cartilage degradation in arthritis (RA) (Van Bezooijen et al., Ann. Rheum. Dis., 61(10):870-876 (Oct. 2002).

8. Normal human bronchial epithelial (NHBE) cells endogenously express zcytor14, IL-17R, and zcytor12, but only neglible amounts of zcytor18 and no detectable amounts of zcytor21. NHBE cells are known to respond to both IL-17 and IL-17F (see, for example, Kawaguchi et al., J. Immunol., 167:4430-4435 (2001)). In addition, NHBE cells express elevated levels of IL-6 and IL-8, well-known pro-inflammatory cytokines (Badolato et al., Semin. Arthritis Rheum. 26(2):526-538 (Oct. 1996); Eur. J. Pediatr., 160(8):457-463 (Aug. 2001)), upon stimulation with IL17 or IL-17F.

9. Exhibit A shows that the addition of 0.7μM soluble zcytor14 receptor (extracellular domain of SEQ ID NO:2) was able to reduce to background levels the up-regulation of IL-6 in NHBE cells caused by the addition of 0.016μM IL-17. On the other

hand, the addition of 0.016μM IL-17 up-regulated IL-6 production in the presence of 0.7μM soluble IL-17R, 0.7μM soluble zcytor12, buffer control, and no add. Thus, I submit that soluble zcytor14 neutralizes IL-17's ability to up-regulate IL-6.

10. Exhibit B shows that the addition of 0.7μM soluble zcytor14 receptor (extracellular domain of SEQ ID NO:2) was able to reduce to background levels the up-regulation of IL-8 in NHBE cells caused by the addition of 0.016μM IL-17. On the other hand, the addition of 0.016μM IL-17 up-regulated IL-8 production in the presence of 0.7μM soluble IL-17R, 0.7μM soluble zcytor12, buffer control, and add. Thus, I submit that soluble zcytor14 neutralizes IL-17's ability to up-regulate IL-8.

11. As a result of the experimental evidence (paragraphs 5, 6, 9, and 10) and the reasoning discussed above (paragraphs 4, 7, and 8), I submit that the zcytor14 polypeptides of U.S. Application Serial No. 09/608,918 are able to initiate or sustain the inflammatory process by up-regulating, for example, IL-17R (paragraph 6). By the same token, a soluble zcytor14 receptor is able to inhibit inflammation by suppressing the inflammatory effects of IL-17 by inhibiting its up-regulation of IL-6 (paragraph 9) and IL-8 (paragraph 10). Thus, I submit that zcytor14 has a specific, credible, and substantial real-world use.

12. I further declare that statementsmade herein of my knowledge are true, and that all statements made on information are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: December 17, 2002 By: Jennifer Pan-Hou

Exhibit A

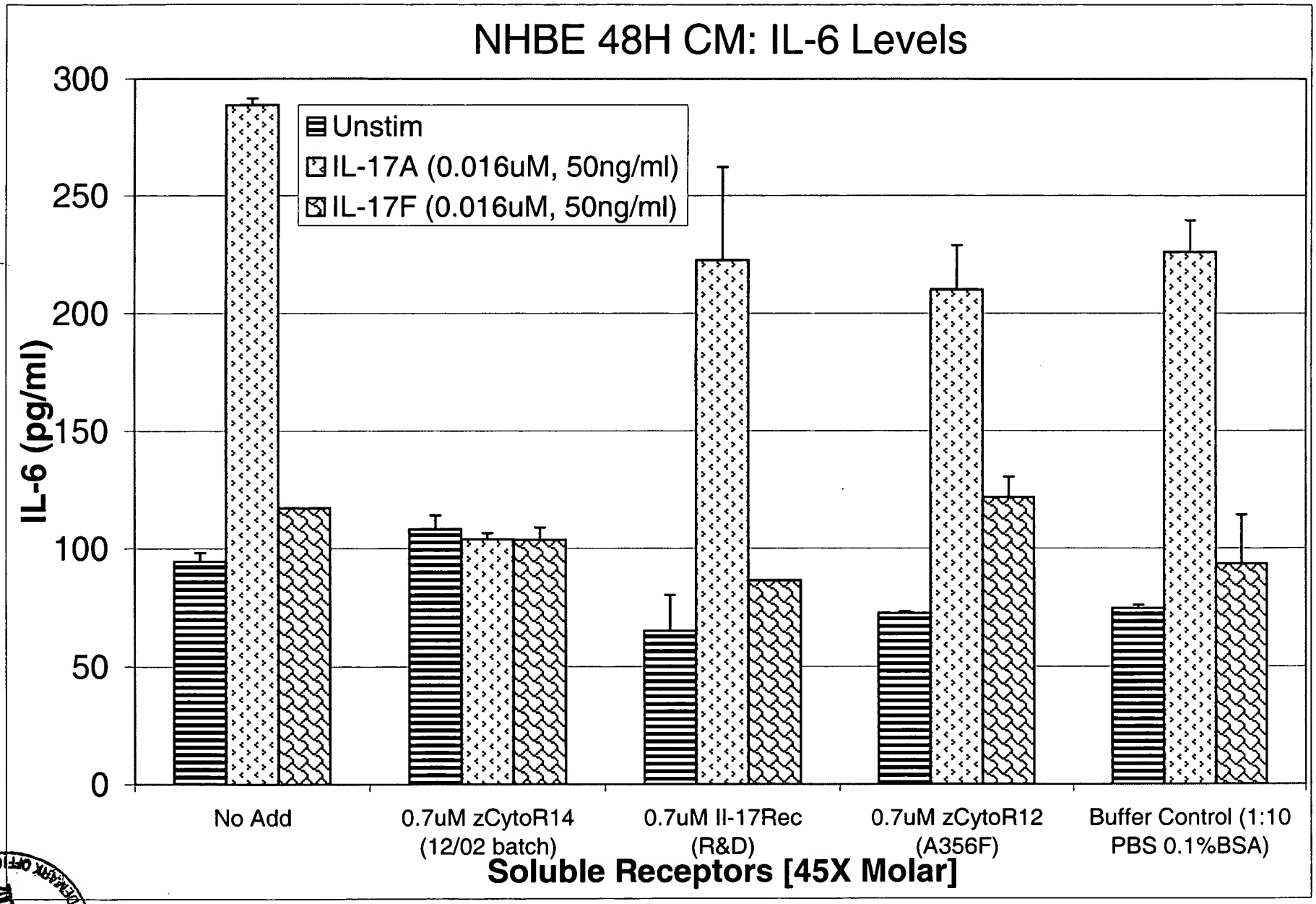

Exhibit B